REMARKS

In a second, non-final Office Action dated November 16, 2007, the Examiner challenged Applicants' priority claim, rejected the claims for obviousness-type double patenting, rejected some claims as anticipated by US Patent No. 5,358,776 and rejected some claims as obvious over combinations of US Patent Nos. 5,358,776, 6,265,153 and 6,762,059. The Examiner acknowledged that Claims 19 and 41 are outside the scope of the cited art.

Applicants respond to each rejection below. In view of the amendments noted above and the remarks presented herein, Applicants respectfully request reconsideration of the merits of this application and respectfully request timely mailing of a Notice of Allowance.

Claim Amendments

Applicants amend Claims 1, 25 and 48 to clarify that the polymeric molecule is provided in a laminar-flowing liquid and to ensure antecedent basis for the liquid in step (b). Applicants also amend Claims 34-35, 46-47, and 69-70 to ensure consistency with the claims from their parent claims. Applicants further amend Claim 48 to recite that polymeric molecules are separated by molecular weight "within the laminar flow."

Priority Claim

The Examiner maintained that the asserted priority documents (*i.e.*, US Provisional Patent Application No. 60/419,884 and US Patent Nos. 5,720,928, 6,294,136 and 6,610,256) do not sufficiently support "separate the elongated molecules by their relative speeds within the laminar flow" as recited in Claims 49-70. The Examiner accorded Claims 49-70 a priority date of October 17, 2003, the application filing date.

Paragraphs [0030] - [0031] of US Provisional Patent Application No. 60/419,884, filed on October 18, 2002, provide the requisite specific support for Claims 49-70 and form the basis for paragraph [0021] in the application. Further, this language provides early support and priority for manipulation in microchannels of polymeric molecules using laminar flow, as recited in each pending claim. These paragraphs note that microchannels may be constructed with "varying cross-sections to promotes a gradient in laminar flow rate," which then may be used to sort "molecules by length, taking advantage of differences in diffusion rate of the ends of the molecule as a function of molecular length."

The Examiner also maintained that the asserted priority documents do not sufficiently support "periodically reversing the flow to cause the polymeric molecules to hover in an elongated/aligned state" as recited in Claims 10-16, 32-38 and 50-56. The Examiner accorded Claims 10-16, 32-38 and 50-56 a priority date of October 17, 2003, the application filing date.

Because this application properly claims the benefit of US Provisional Patent Application No. 60/419,884, Applicants respectfully request that all claims, including Claims 49-70, be accorded the priority date of October 18, 2002 for at least the inventive concept of manipulating polymeric molecules in a microchannel using laminar flow.

Rejections for Non-Statutory Obviousness-Type Double Patenting

The Examiner maintained rejections for obviousness-type double patenting. Claims 1, 4-7, 17, 25, 28-31, 39 and 45-48 were rejected over Claim 1 of US Patent No. 7,049,074 to Schwartz (hereinafter, Schwartz I), and Claims 1, 3-7, 17, 23-25, 27-31, 39 and 45-48 were rejected over Claims 1-2, 10, 12-13, 15-16 and 26-27 of US Patent No. 6,509,158 to Schwartz (hereinafter, Schwartz II). The Examiner alleged that Schwartz I and II render the rejected claims obvious by generally disclosing methods of elongating, fixing and characterizing polymeric molecules on a solid planar surface with a positive charge.

The Examiner focused upon differences among surfaces to which polymeric molecules can be fixed but overlooked the patentably distinct concepts of elongating (Claim 1), aligning (Claim 25) and separating (Claim 48) polymeric molecules during their passage in a laminar-flowing liquid through a microchannel in the first instance. This concept is neither disclosed nor claimed in Schwartz I and II, in which elongated polymeric molecules using gel inserts and electrophoresis outside of microchannels. Although both Schwartz I and II showed previously-elongated polymeric molecules entering laminar flow devices (*see, e.g.*, Fig. 25 of either document), neither contemplated or disclosed elongating, aligning or separating polymeric molecules using laminar flow during passage through a microchannel.

This aspect was unknown in the art until Applicants appreciated that laminar flow alone could elongate polymeric molecules passing through microchannels. The Examiner identified no passage in either patent disclosing, suggesting or hinting at this fundamentally different approach and provided no basis for alleging that this approach would have been apparent to a person having ordinary skill in the art.

While an obviousness-type double patenting rejection is based upon the claims of a cited document, an Examiner must interpret the scope and meaning of the claims in light of the entire disclosure of that document. *See*, MPEP § 804 II.B.1.; *see also*, *In re Vogel*, 422 F.2d 438, 441-442 (CCPA 1970). In Schwartz I and II, laminar flow was used to move polymeric molecules into a laminar flow device for subsequent viewing or manipulation (*i.e.*, fixing to the planar surface) but only after the polymeric molecules were elongated using gel inserts and electrophoresis (*see*, Section 5.1.3 and Fig. 25) prior to entering the microchannel.

The same holds true as it relates to the claimed methods for aligning and methods for separating polymeric molecules, since each relies initially upon laminar flow to accomplish the alignment and separation. In contrast, polymeric molecules were elongated, aligned and separated in Schwartz I and II on the basis of transit through gel inserts, not upon subsequent transit into a laminar flow device after emergence from gel inserts for subsequent viewing or manipulation.

In view of these remarks, Applicants respectfully request reconsideration of the rejections for obviousness-type double patenting.

Rejections Under 35 U.S.C. § 102

The Examiner rejected Claims 1-7, 25-31, 48 and 62-64 under 35 U.S.C. § 102(b) as anticipated by US Patent No. 5,356,776 to Kambara *et al.* The Examiner alleged that Kambara teaches a method of elongating polymeric molecules that anticipates Claim 1, a method of aligning polymeric molecules that anticipates Claim 25 and a method for separating polymeric molecules of differing molecular weights that anticipates Claim 48. Applicants respectfully disagree.

Kambara does not disclose every limitation and element as recited in the pending claims. Specifically, MPEP § 2131 provides:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (noting that the identical invention must be shown in as complete detail as is contained in the claims) (emphasis added); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed.Cir. 1989) (noting that the elements must be arranged as required by the claim).

With respect to Claims 1, 25, 48 and their dependents, Kambara did not disclose passing polymeric molecules in a laminar-flowing liquid through a microchannel to elongate, align or separate the molecules. The Examiner pointed to no disclosure in Kambara showing or contemplating laminar flow. No example in Kambara used laminar flow and Kambara nowhere mentioned laminar flow.

Instead, Kambara used fluid flow associated with electrophoresis (presumably, sheath flow, electroosmotic flow and capillary/convective flow) to manipulate the molecules (*see*, Abstract; FIGS. 2, 4-6 and 10; Column 2, lines 46-55; Column 2, line 65 to Column 3, line 2; Column 5, line 56 to Column 6, line 17; and Examples 1-4). One of ordinary skill in the art understands that fluid flow during electrophoresis is not laminar flow. Particles dispersed in a fluid for electrophoresis typically carry an electric surface charge. These charged particles drag fluid as they move in the electric field, but this fluid flow is not laminar flow. Often such flow is a capillary flow or convective flow. As noted above, Applicants were the first to appreciate that laminar flow could elongate polymeric molecules during passage through a microchannel.

In Example 1, Kambara elongated polymeric molecules during electrophoresis through an agarose gel (*see*, FIG. 2; Column 6, lines 45-49). In Example 2, Kambara elongated polymeric molecules during electrophoresis by the diameter of spewing outlets as they exited the outlets (*see*, FIG. 4 and Column 8, lines 46-53 in particular). In Example 3, Kambara elongated polymeric molecules during electrophoresis by the diameter of fine grooves as they exited the grooves (*see*, FIG. 5 and Column 9, lines 5-11 in particular). In Example 4, Kambara elongated polymeric molecules during electrophoresis by the diameter of molecular sieves as they exited the sieves (*see*, FIG. 6 and Column 9, lines 18-23).

The same holds for Kambara's methods for elongating polymeric molecules attached to particles in fluid flow associated with electrophoresis (*see*, Figs. 8-9; Column 3, line 48 to Column 4, line 65; Examples 4-6). In Example 4, Kambara fixed polymeric molecules at one end to a matrix and elongated (*see*, Column 10, lines 24-47). Also in Example 4, Kambara fixed polymeric molecules at one end to a particle having a diameter between about 0.2 μm to 10 μm, such that the particles would not pass through apertures during electrophoresis (*see*, Column 9, lines 48-65). Likewise, in Example 5, Kambara fixed polymeric molecules at one end to a fixing particle (*i.e.*, a polystyrene particle) have a 1 μm diameter and elongated using electrophoresis (*see*, Column 12, lines 22-66). Query how laminar flow can occur when a particle is stuck in a

blocked aperture? In Example 6, Kambara fixed polymeric molecules having avidin-coated microparticles at one end to quartz and elongated with electrophoresis (*see*, Column 14, lines 3-15).

With respect to Claim 25 and its dependents, Applicants reiterate their comments above, and specifically note that alignment, if any, would have been caused by the agarose gel or the diameter of spewing outlets, the fine grooves or the molecular sieves. Elsewhere in the Office Action, the Examiner admits that Kambara did not align molecules in a passage or channel. Moreover, the claims recite that a plurality of polymeric molecules are aligned during passage through a microchannel. The spewing outlets, the fine grooves and the molecular sieves allow only a single polymeric molecule to be aligned at a time.

With respect to Claim 48 and its dependents, Applicants reiterate their comments above, and specifically note that separation, if any, would have been caused by the agarose gel or the diameter of spewing outlets, the fine grooves or the molecular sieves.

Moreover, the pending claims specifically recite that polymeric molecules are separated during passage through a microchannel; however, the spewing outlets, the fine grooves and the molecular sieves allow only one polymeric molecule to be separated at a time and no example used laminar flow to separate polymeric molecules during passage through a microchannel.

In view of these remarks, Applicants respectfully request reconsideration of this rejection as applied to Claims 1, 25, 48 and their dependent claims.

Rejections Under 35 U.S.C. § 103

The Examiner rejected Claims 8-9, 17-18, 21-24, 39-41, 43-46 and 58-61 under 35 U.S.C. § 103(a) as obvious over Kambara, *supra*, in view of US Patent No. 6,265,153 to Bensimon *et al.* The Examiner alleged that although Kambara does not disclose aligning or staging polymeric molecules within a passage or channel and that although Kambara does not disclose that a wall can be electrostatically attractive to polymeric molecules, it would have been obvious to one of ordinary skill in the art after reading Bensimon. Applicants respectfully disagree. Applicants' invention distinguishes over the cited documents at least by its use of laminar flow to elongate, align or separate polymeric molecules during passage through a microchannel.

As noted above, Kambara failed to contemplate or disclose using laminar flow to elongate, align or separate polymeric molecules during passage through a microchannel. At best, Kambara teaches *arguendo* that polymeric molecules can be elongated, aligned or separated by electrophoresis or by non-laminar fluid flow resulting from electrophoresis. Likewise, Kambara showed that apertures (*i.e.*, as shown in Kambara 's spewing outlets, fine grooves and molecular sieves) having a size slightly larger than a polymeric molecule (either free of or attached to a particle) can be used to manipulate polymeric molecules. As such, Applicants reiterate their previous remarks and point out that Kambara cannot render the pending claims obvious, since the elements of Claims 1, 25 and 48 are neither anticipated by, nor obvious in view of Kambara.

Bensimon does not cure the deficiencies of Kambara and provides the skilled artisan with no motivation to combine with Kambara. As Applicants have noted in a prior persuasive response, Bensimon does not disclose using laminar flow to elongate, align or separate polymeric molecules during passage through a microchannel. Bensimon, like Kambara, did not disclose laminar flow fluid dynamics, which causes polymeric molecules to elongate, align or separate at a leading edge of a fluid. In contrast, Bensimon disclosed using capillary action/convection (principally caused by evaporation at a trailing edge of a solution) to create a meniscus that elongates, aligns or separates polymeric molecules attached to a surface. *See* Fig. 6 of Bensimon and Column 2, lines 59-68; Column 17, lines 41-45; and Column 19, lines 30-32; as well as Example 1, Column 1, lines 39-46 of Bensimon. Bensimon teaches away from using laminar flow by expressly noting that the flow types used by Applicants are not as efficient as a meniscus. *See*, Column 4, lines 7-20. Moreover, Bensimon failed to disclose microchannels -- the structures formed by a pair of cover slips in Bensimon lack sides and are not microchannels. Because Bensimon failed to disclose these elements, it cannot render the pending claims obvious, since the elements of Claims 1, 25 and 48 are neither anticipated by, nor obvious in view of Bensimon, alone or in combination with Kambara. In view of these remarks, Applicants respectfully request reconsideration of this rejection as applied to Claims 8-9, 17-18, 21-24, 39-41, 43-46 and 58-61.

The Examiner also rejected Claims 10-16, 20, 32-38, 42, 49-57 and 65-70 as obvious over Kambara, *supra*, in view of Bensimon, *supra*, in further view of US Patent No. 6,762,059 to Chan *et al.* The Examiner admitted that Kambara and Bensimon do not disclose periodically reversing the flow to cause polymeric molecules to hover in an elongated state, but alleged that

this would have been obvious to one of ordinary skill in the art after reading Chan. Applicants respectfully disagree. Applicants' invention distinguishes over the cited documents at least by the use of laminar flow to elongate, align or separate polymeric molecules during passage in a microchannel.

As noted above, Kambara and Bensimon failed to contemplate or disclose using laminar flow to elongate, align or separate polymeric molecules during passage in a microchannel. As such, Applicants reiterate their previous remarks and point out that Kambara and Bensimon cannot render the pending claims obvious, since the elements of Claims 1, 25 and 48 are neither anticipated by, nor obvious in view of Kambara and Bensimon.

Chan does not cure the deficiencies of Kambara and Bensimon. As noted in Applicants' previous response, Chan does not disclose using laminar flow to elongate, align or separate polymeric molecules. The fluid dynamics of Chan, like Kambara and Bensimon, are not laminar flow. In contrast, Chan disclosed devices having structures (*e.g.*, funnels, posts, branches and serial structures) to elongate nucleic acids. *See*, Figs. 3-4, 11-24, and 36; *see also*, Column 15, lines 42-62; Section 5.4.1; and Section 5.5.1 of Chan. More importantly, these structures prevent laminar flow, and instead create turbulent flow (*see*, Column 28, lines 5-21 of Chan). Thus, Chan did not use laminar flow to elongate, align or separate polymeric molecules during passage through a microchannel for subsequent analysis. Because Chan failed to disclose these elements, it cannot render the pending claims obvious, since the elements of Claims 1, 25 and 48 are neither anticipated by, nor obvious in view of Chan, alone or in combination with Kambara and Bensimon.

The Examiner alleged that Chan disclosed periodically reversing flow to cause a polymeric molecule, like a nucleic acid molecule, to hover in an elongated state. However, as noted in Applicants' previous response, Chan used an electrical field to move polymeric molecules in a fluid. In fact, Chan noted that the electrical field should "not necessarily [act] on the surrounding fluid at all (if it is uncharged)." *See*, Column 40, lines 41-45 of Chan. Chan also stated that the "polymers then follow electric field lines instead of flow lines." *See*, Column 40, lines 48-52 of Chan. Thus, Chan do not actually use reverse fluid flow. In fact, Chan teaches away from Applicants' methods, as it noted that fluid flow in the opposite direction can be damaging to stretching. In contrast, the claimed methods reverse laminar flow, not an electrical field, to cause the nucleic acid to hover. While Applicants can use an electric field, it is only to

adsorb polymeric molecules to a wall of a microchannel. As such, Chan does not contemplate or disclose periodically reversing laminar flow to cause a polymeric molecule to hover and therefore cannot not render Claims 1, 25 and 48 or the claims that depend therefrom obvious. To clarify this distinction, Applicants amend Claims 10-11, 32-33 and 51 to recite that "laminar" flow is reversed to cause the polymeric molecules to hover. Support for this amendment is found in paragraphs [0015] and [0090], Fig. 16 and Claim 50 of the application. In view of the amendments noted above and these remarks, Applicants respectfully request reconsideration of this rejection as applied to Claims 10-16, 20, 32-38, 42, 49-57 and 65-70.

Fees

A petition for a two-month extension of time accompanies this response so that it will be deemed to have been timely filed. No other extension of time is believed due; however, if any additional extension is due, in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055. Likewise, no additional fees are believed due; however, if any fees are due, in this or any subsequent response, please charge Deposit Account 17-0055.

Respectfully submitted,

/Brian C. Cholewa/
Brian C. Cholewa
Reg. No. 58,392
Attorney for Applicants
QUARLES & BRADY LLP
P.O. Box 2113
Madison, WI 53701-2113

TEL (608) 251-5000
FAX (608) 251-9166